REMARKS

Claims 27-40 are pending in the subject application. By this Amendment, applicants have amended claims 27-30, 33-36, and 39. Support for the amendments to claim 27 can be found in the specification as originally filed at page 16, lines 3 to 13 and line 20; page 83, lines 7 to 16; and Fig. 13. Support for the amendments to claim 28 can be found in the specification as originally filed at page 16, line 20; page 16, line 35 to page 17, line 10; page 83, lines 7 to 16; and Fig. 13. Support for the amendments to claim 29 can be found in the specification as originally filed at page 19, lines 17-19. Support for the amendments to claim 30 can be found in the specification as originally filed at page 19, lines 19-21. Support for the amendments to claim 33 can be found in the specification as originally filed at page 19, line 25 to page 20, line 5; page 83, lines 7 to 16; and Fig. 13. Support for the amendments to claim 34 can be found in the specification as originally filed at page 20, lines 12-14. Support for the amendments to claim 35 can be found in the specification as originally filed at page 20, lines 17-19. Support for the amendments to claim 36 can be found in the specification as originally filed at page 20, lines 19-21. Support for the amendments to claim 39 can be found in the specification as originally filed at page 22, lines 1-3, and page 83, lines 7-16.

After entry of this Amendment, claims 27-40 will still be pending and under examination.

Rejection Under 35 U.S.C. §112, First Paragraph (Enablement)

The Examiner rejected claims 27-38 and 40 under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification. The Examiner stated that the specification, while being enabling for an *in vitro* method of increasing a target cell's susceptibility to DNA damaging agents comprising the administration of antisense that inhibit the expression of human Ku70, does not reasonably provide for *in vivo* methods.

In response, applicants respectfully traverse the Examiner's rejection.

As far as the rejection applies to claim 27, applicants have hereinabove amended claim 27 to recite that the method is an *in vitro* method. Based on the Examiner's comments in the January 11, 2007 Final Office Action, applicants understand the Examiner to agree that claim 27 as amended hereinabove is be enabled by the specification.

With regard to independent claims 28 and 33, applicants note that the Examiner has stated that "[c]ontrary to applicants' assertions, the specification teaches an increase in radiation and chemotherapeutic sensitivity in Ku70 cells obtained from Ku70 knockout mice. This is not representative of the ability to successfully deliver adequate quantities of antisense targeting human Ku70 to an organism, whereby treatment effects are

provided". Applicants respectfully draw the Examiner's attention, however, to page 83, lines 1-10 of the specification which teach antisense constructs of Ku70 cDNA in the antisense orientation (also see Fig. 13 and the description thereof in the specification at page 12, lines 5 to 9). Moreover, the specification teaches that expression of the Ku70 antisense increased the toxic effects of adriamycin and increased the cytotoxic effect of gamma radiation (see page 83, lines 11-16) in HeLa cells (i.e. human cells). Thus, applicants maintain that the specification enables one of ordinary skill in the art to make and use the invention as presently claimed. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

The Examiner asserted, noting applicants' position that Au Young et al. (U.S. 5,773,580) teach adenoviral mediated delivery of nucleic acids, that the ability to provide treatment effects in an organism by administering antisense requires undue experimentation beyond that provided in the instant disclosure and in the art. The Examiner stated, inter alia, that the efficacy of both the antisense and an appropriate delivery device must be tested empirically, and the ability to provide treatment effects in an organism using antisense is a highly unpredictable endeavor.

Applicants note that the methods as claimed in amended claims 28 and 33 require the antisense oligonucleotide which has the sequence of a human Ku70 cDNA in the antisense orientation and

is introduced into the subject via an adenoviral vector comprising an expression vector encoding the antisense oligonucleotide under the control of a heat shock promoter. Applicants maintain that in light of the success of in the specification as recited hereinabove of the specific antisense recited in the claimed methods and the prior successes of adenoviral mediated delivery as described in applicants' Amendment filed on October 13, 2006 in connection with the above-identified application, one of ordinary skill in the art would be able to make and use the invention as claimed based on applicants' disclosure. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Rejections Under 35 U.S.C. §103(a)

The Examiner rejected claims 27, 39 and 40 as allegedly obvious over Reeves et al. (J. Biol. Chem., Vol. 26499):5047-5052, 1989) and Milner et al. (Nature Biotech. 15:537-541, 1997), the combination in view of Taniguchi et al. (actually Takiguchi et al.) (Genomics, 35:129-135, 1996) and AuYoung et al. (U.S. Patent No. 5,773,580) insofar as the claims are drawn to compositions and methods for increasing a target cell's sensitivity to DNA damaging agents in vitro comprising the administration of an antisense oligonucleotide in an adenoviral expression vector comprising a heat shock promoter, which antisense specifically hybridizes with a nucleic acid encoding a DNA-dependent protein kinase subunit (Ku70) which antisense

inhibits the expression of the target ku70 subunit.

In response, applicants respectfully traverse the Examiner's rejection.

Applicants note that the Examiner has stated that the efficacy of an antisense must be tested empirically, thus indicating that the efficacy of any one antisense molecule is not predictable. Applicants maintain that the claimed method recites an antisense molecule empirically determined only by applicants to be efficacious, and not taught or suggested by the combination of cited prior art. In addition, applicants note that predictability, with respect to reasonable expectation of success, is determined at the time the invention was made (see M.P.E.P. §2143.02). Applicants note that the Examiner has stated that the antisense must be tested empirically, i.e. that the art is not predictable. Thus, the prior art, which does not provide the antisense recited in the claimed methods, does not provide a reasonable expectation of success of the claimed method.

In addition, applicants also note that nowhere in the cited combination of references is an antisense oligonucleotide having the sequence of a human Ku70 cDNA in the antisense orientation taught or suggested.

Applicants thus maintain that the invention as claimed is not obvious over the combination of cited prior art. Accordingly, applicants respectfully request that the Examiner reconsider and

withdraw this ground of rejection.

Provisional Obviousness-Type Double Patenting Rejection

In the January 11, 2007 Final Office Action, the Examiner provisionally rejected claims 27, 39 and 40 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1, 15, 16 and 18-22 of copending U.S. Application No. 09/750,410.

Applicants understand that this is only a provisional rejection, and will consider filing a Terminal Disclaimer if necessary should the rejection become non-provisional.

Conclusion

For the reasons set forth above, applicants respectfully request that the Examiner reconsider and withdraw the rejections, and solicit allowance of pending claims 27-40.